WEST NILE VIRUS *(notifiable as ENCEPHALITIS)*

DISEASE REPORTING

In Washington

West Nile virus (WNV) infections in humans were first reported in the United States in 1999. Since that time, infection of reservoir birds and vector mosquito species has spread from the east coast through the south and Midwest, and over 4,100 human cases were reported from more than 35 states during 2002. The first case of WNV infection reported in a Washington resident occurred in a Skagit County resident exposed while visiting in Michigan in the summer of 2002.

Purpose of reporting and surveillance

- To assist in the diagnosis of cases.
- To distinguish WNV infections acquired locally from those related to travel.
- To better understand the epidemiology of these infections in Washington State and target mosquito control measures.
- To identify emerging infections in Washington.

Reporting requirements

- Health care providers: notifiable to Local Health Jurisdiction within 3 work days
- Hospitals: notifiable to Local Health Jurisdiction within 3 work days
- Laboratories: no requirements for reporting
- Local health jurisdictions: notifiable to DOH Communicable Disease Epidemiology within 7 days of case investigation completion or summary information required within 21 days.

Clinical criteria for diagnosis

WNV infection may result in a febrile illness of variable severity associated with neurologic symptoms ranging from headache to aseptic meningitis or encephalitis. WNV encephalitis cannot be distinguished clinically from other central nervous system (CNS) infections. Symptoms can include headache, confusion or other alteration in sensorium, muscle weakness, arthralgias and myalgias, nausea, and vomiting. Signs may include fever, rash, lymphadenopathy, meningismus, cranial nerve palsies, paresis or paralysis, sensory deficits, altered reflexes, convulsions, abnormal movements, and coma of varying degree. Only infections resulting in encephalitis or meningitis are reportable.

Laboratory criteria for diagnosis

- Fourfold or greater change in serum antibody titer, or
- Isolation of virus from or demonstration of viral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid, or
- Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF by antibody-capture enzyme immunoassay (EIA), or
- Virus-specific IgM antibodies demonstrated in serum by antibody-capture EIA and confirmed by demonstration of virus-specific serum immunoglobulin G (IgG) antibodies in the same or a later specimen by another serologic method (e.g., neutralization or hemagglutination inhibition).

Case definition

- Probable: a clinically compatible case occurring during a period when arboviral transmission is likely, and with the following supportive serology: 1) a single or stable but elevated titer (≤ twofold change) of virus-specific serum antibodies; or 2) serum IgM antibodies detected by antibody-capoture EIA but with no available results of a confirmatory test for virus-specific serum IgG antibodies in the same or a later specimen.
- Confirmed: a clinically compatible case that is laboratory confirmed.

Because closely related arboviruses exhibit serologic cross-reactivity, positive results of serologic test using antigens from a single arbovirus can be misleading. In some circumstances (e.g., in area where two or more closely related arboviruses occur, or in imported arboviral disease cases), it may be epidemiologically important to attempt to pinpoint the infecting virus by conducting cross-neutralization tests using an appropriate battery of closely related viruses. This is essential, for example, in determining that antibodies detected against St. Louis encephalitis are not the result of an infection with West Nile (or dengue) virus, or vice versa, in areas where both of these viruses occur.

A. DESCRIPTION

1. Identification

Most WNV infections are asymptomatic; mild cases often occur as a febrile headache or aseptic meningitis with symptoms lasting about 3-6 days. About 20% of infected persons will develop fever and mild symptoms, and approximately 1/150 will develop serious neurological disease involving parts of the brain, spinal cord and meninges. Signs and symptoms of this disease cannot be reliably distinguished from other arboviral infections, however in the initial 1999 US outbreak, more than 50% of the hospitalized patients had severe muscle weakness, and some were initially thought to have Guillian-Barre syndrome. In earlier outbreaks, the disease has been described as an acute febrile illness with malaise, anorexia, nausea, vomiting, headache, eye pain, myalgias, rash and lymphadenopathy. Severe infections may progress to meningitis and/or encephalitis, but may have an atypical presentation with ataxia, extrapyramidal signs, cranial nerve

abnormalities, myelitis, optic neuritis, polyradiculitis and seizures. Risk for severe infection appears greatest with increasing age, as does risk for fatality: case-fatality rates range from 4% to 14%, but among hospitalized patients over 70 years of age, case-fatality rates are 15-29%. Few data exist on long-term outcome after serious infection, but small studies in New York suggest that long-term sequelae, including neurologic deficits are not uncommon among survivors.

Like other arboviral infection, WNV disease requires differentiation from the tickborne encephalitides; encephalitic and nonparalytic poliomyelitis; rabies; mumps meningoencephalitis; lymphocytic choriomeningitis; aseptic meningitis due to enteroviruses; herpes encephalitis; postvaccinal or postinfection encephalitides; and bacterial, mycoplasmal, protozoal, leptospiral and mycotic meningitides or encephalitides. Venezuelan equine encephalomyelitis and Rift Valley fever viruses, like WNV, produce primarily arthropod-borne viral fever, but may sometimes cause encephalitis.

Identification is made by demonstrating specific IgM in acute-phase serum or CSF, or antibody rises between early and late specimens of serum by neutralization, CF, HI, FA, ELISA or other serologic tests. Cross reactions may occur within a virus group. Virus may occasionally be isolated by inoculation of suckling mice or cell culture with the brain tissue of fatal cases, rarely from blood or CSF after symptoms have appeared; histopathologic changes are not specific for individual viruses.

2. Infectious Agent

West Nile virus is a single-stranded RNA virus of the *Flaviviridae* family (*Flavivirus*), and is part of the Japanese encephalitis virus serocomplex, which contains several important human encephalitis viruses: Japanese encephalitis, St. Louis encephalitis (SLE), Murray Valley encephalitis, and Kunjin. Flaviviruses may cross-react serologically – in the US, the two most important cross-reactions occur between WNV and SLE.

3. Worldwide Occurrence

Until 1999, WNV was found only in the Eastern Hemisphere, with wide distribution in Africa, Asia, the Middle East, and Europe. The virus was first isolated and identified in 1937 from an infected woman in the West Nile district of Uganda. Human outbreaks occur, and have been more frequent and associated with more severe neurological disease since the mid-1990s. Recent outbreaks in Romania, Israel, Russia, and the eastern and southern US involved hundreds of cases with significant neurological disease.

4. Reservoir

Due to the recent introduction of WNV in the US, investigation of the ecology of the virus in the Western Hemisphere is still ongoing. WNV has been detected in 29 North American mosquito species. *Culex pipiens*, *Culex restuans*, and *Culex quinquefaciatus* appear to be the most important maintenance vector in the eastern U.S, but it is not known which species are the most critical for transmission to humans. The virus is maintained in

an enzootic cycle involving migratory birds and mosquitoes, with mosquitoes that bite both humans and birds acting as "bridge vectors." Humans and other mammals (primarily horses) are incidentally infected, and do not function as reservoirs for mosquito infection.

5. Mode of Transmission

By the bite of infective mosquitoes. Although *Culex* species are known to carry the virus in the US, the most important vector species for WNV transmission to humans are unknown.

6. Incubation period

Not precisely known, probably 3-14 days.

7. Period of communicability

Not directly transmitted from person to person. Although data regarding WNV is limited, for other arboviral diseases, virus is not usually demonstrable in the blood of humans after onset of disease. Mosquitoes remain infective for life. Viremia in birds usually lasts 2-5 days, but may be prolonged in bats, reptiles and amphibians, particularly if interrupted by hibernation. Horses develop active disease with the two equine viruses and with JE, but viremia is rarely present in high titer or for long periods; therefore, humans and horses are uncommon sources of mosquito infection.

8. Susceptibility and resistance

Susceptibility to symptomatic disease increases with age, and risk for serious infection is usually highest among the elderly, and possibly, among some persons with immunosuppression or diabetes mellitus.

B. METHODS OF CONTROL

1. Preventive measures:

a. Educate the public as to the modes of spread and control.
b. Destroy larvae and eliminate breeding places of known and suspected vector mosquitoes, e.g., eliminate standing water near areas of human habitation to prevent breeding of WNV vectors.
c. Kill mosquitoes by space and residual spraying of human habitations (also see MALARIA, B1(I)a-c).
d. Screen sleeping and living quarters; use mosquito bed nets.
e. Avoid exposure to mosquitoes during hours of biting, or use DEET-containing repellents (see MALARIA, B1(II)1-4).
f. In endemic areas, immunize domestic animals or house them away from living quarters, e.g., horses in WNV endemic areas.

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority as encephalitis.
b. Isolation: None; virus is not usually found in blood, secretions or discharges during clinical disease. Enteric precautions are appropriate until enterovirus meningoencephalitis is ruled out.
c. Concurrent disinfection: None.
d. Quarantine: None.
e. Immunization of contacts: None.
f. Investigation of contacts and source of infection: Search for missed cases and the presence of vector mosquitoes. Primarily a community vector control problem (see B3, below).
g. Specific treatment: None.

3. Epidemic measures

a. Identification of infection among horses or birds and recognition of human cases in the community have epidemiologic value by indicating frequency of infection and areas involved. Immunization of horses probably does not limit spread of the virus in the community.
b. Fogging or spraying from aircraft with suitable insecticides has shown promise for aborting urban epidemics of SLE, however, efficacy against WNV is unknown.

4. International measures

Spray with insecticide those airplanes arriving from recognized areas of prevalence. WHO Collaborating Centres.